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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/693,999

10/28/2003

Iliia Davydov

2528-10

4116

23117

7590

07/26/2006

NIXON & VANDERHYE, PC
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ARLINGTON, VA 22203

EXAMINER

DESAI, ANAND U

ART UNIT

PAPER NUMBER

1653

DATE MAILED: 07/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/693,999	Applicant(s) DAVYDOV ET AL.	
	Examiner Anand U. Desai, Ph.D.	Art Unit 1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 June 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 3-8, 10, 12, 15-17, 35-47, 55 and 57-63 is/are pending in the application.
- 4a) Of the above claim(s) 5-8, 10, 12, 15, 16, 35-47 and 55 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 3, 4, 17 and 57-63 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Amendment

1. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn. This office action is in response to Amendment filed on June 29, 2006. Claims 1, 2, 9, 11, 13, 14, 18-34, 48-54, and 56 have been previously cancelled. Claims 5-8, 10, 12, 15, 16, 35-47, and 55 have been previously withdrawn. Claims 3, 4, 17, 57-63 are currently pending and are under examination.

Withdrawal of Rejections

2. The rejection of claims 3, 4, 17, and 57-63 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement because of new matter is withdrawn.

3. The rejection of claims 3, 4, 17, 57-63 under 35 U.S.C. 112, second paragraph is withdrawn.

4. The rejection of claims 3, 4, 17, and 57-63 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn.

5. The rejection of claims 57-59, 62, and 63 under 35 U.S.C. 102(b) as being anticipated by Morishima-Kawashima, M. et al. (Neuron 10(6): 1151-1160 (1993)) is withdrawn.

New Rejection

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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7. Claims 3, 4, 17, and 57-63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). The term “complex” in claims 3, 4, 17, and 57-63 is used by the claim to mean covalent attachment of ubiquitin or a derivative thereof with a protein formed by N-end rule ubiquitylation (see [0050]), while the accepted meaning is a “conjugate”, which would describe the covalent bond formed between a protein and the ubiquitin or derivative thereof. Suggest describing “An isolated conjugate complex comprising at least one ubiquitin...”

Maintenance of Rejections

Claim Rejections - 35 USC § 112

9. Claims 3, 4, 17, and 57-63 stand rejected under 35 U.S.C. 112, first paragraph, scope of enablement.

The rejection is discussed in the office action mailed on June 20, 2005 and February 24, 2006.

Response to Remarks

Applicant states that a person skilled in the art would be able to practice the subject invention without undue experimentation in view of the disclosure in the specification and

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further in view of the high level of skill in the relevant art. Applicants urge that the experimentation required to practice the full scope of the pending claims is routine and not undue because a skilled artisan routinely engages in such experimentation. Applicants urge that consideration of tertiary structure are irrelevant to Applicants' invention because the specification discloses a high-throughput screening method routine in the art which will enable a skilled artisan to evaluate all variants and fragments of interest for the desired N-end rule ubiquitylation.

Applicant's arguments filed June 29, 2006 have been fully considered but they are not persuasive. The claims are drawn to **fragments and derivatives** of a group of proteins that form an isolated conjugate with ubiquitin or derivative thereof. There is unpredictability in the art with regard to the tertiary structure required for the interaction of substrate with the cognate E3 ubiquitin-protein ligase enzymes. There is also a limited understanding of particular E3 ubiquitin ligase active sites that are required for the proper enzyme-substrate interaction (see paragraphs 3 and 6 of the Wands analysis for cited reference). Furthermore, the specification does not disclose the conjugation of a fragment having at least 50 amino acids and at least 90% sequence identity with the corresponding full-length protein to at least one ubiquitin formed via N-end rule pathway. Applicant's disclosure states the recognition sites on E3 ligases appear to be substrate specific, with a lack of general consensus motifs (sentence connecting page 2 and 3). Therefore, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See *In re Wands*, 858 F.2d at 737, 8USPQ2d at 1404 (Fed. Cir. 1988). Thus, absent direction regarding whether the structure of the **fragments and derivative** polypeptides can

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tolerate the modifications contemplated, one of skill in the art would not be able to practice the claimed invention commensurate in scope with the claims.

Conclusion

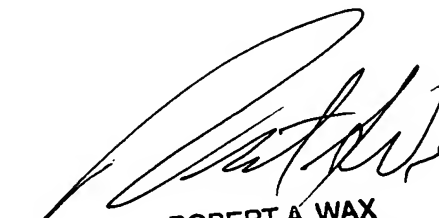
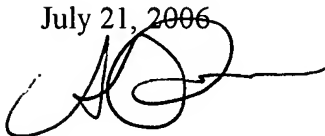
10. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anand U. Desai, Ph.D. whose telephone number is (571) 272-0947. The examiner can normally be reached on Monday - Friday 9:00 a.m. - 5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on (517) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

July 21, 2006



ROBERT A. WAX
PRIMARY EXAMINER